Diabetes in Children and Teens

Mary Murray, MD
Utah Diabetes Center Pediatrics
Update - 2004

Diabetes in Pediatrics

- Incidence
- Etiology
- Prevention
- Treatment

Classification of Diabetes

- Type 1:
  - Immune mediated β-cell destruction leading to absolute insulin deficiency: most common type in children and adolescents
- Type 2:
  - ranges from predominantly insulin resistance with relative deficiency to predominant secretory defect with insulin resistance, becoming much more prevalent in adolescents
- Gestational diabetes
- Other types:
  - Cystic fibrosis, drug induced, genetic syndromes

Criteria to Diagnose Diabetes

- Symptoms of diabetes plus random plasma glucose ≥ 200mg/dl (11.1 mmol/l)

or

- Fasting plasma glucose ≥ 126 mg/dl (7.0 mmol/l)

or

- 2 hour plasma glucose ≥200 mg/dl during OGTT.
  - WHO criteria, glucose load of 1.75 gm/kg or max of 75 gm glucose in water

Diabetes: Incidence

- Incidence of both type 1 and type 2 is increasing world wide
- Type 1 increasing 3-5% per year worldwide
- Type 2 increasing with increasing obesity
  - Prediction that 1/3 of all Hispanic children born in 2003 will develop type 2 diabetes

Characterization of Diabetes

	Type 1	Type 2
Age	Child / Adolescent	Adolescent
Habitus	Lean	Heavy
Acanthosis	No	Yes
Family history/ Ethnicity	Uncommon (5%)/ Caucasion	Common (74-100%) / Minorities
DKA/onset	Common / rapid	Uncommon/ insidious
Insulin dependent	Lifelong	Episodic
Autoimmunity	Common (80% +)	Uncommon (70% -)

Incidence: Type 1 Diabetes

- Incidence is increasing world wide
  - In Finish children ages 0-14 years the incidence has increased from 20 per 100,000 to 50 per 100,000 over the last 40 years.
- Type 1 diabetes is still the more common type of diabetes in Caucasian children and teens
- Type 1 is not related to diet (e.g caloric intake, junk food intake)

Pathophysiology of Type 1

- Type 1 Diabetes:
  - Easy to diagnose, but pathogenesis still not completely understood
  - 2 hit phenomenon:
    - Genetic predisposition
    - Second hit: infection?, environment?
  - Not preventable, not predictable
  - Evolves over weeks to months
- Type 2 is related to lifestyle and obesity
  - Becoming more common in children especially in some ethnic groups

General Information

- Type 1 diabetes is the most common chronic disease of childhood
- Good control of diabetes will decrease the risk of long term complications
  - Most recent information suggests that complication rate has been cut in half in the last 20 years—and we can do better
  - Longer more productive, healthy lives
  - Must invest in the future health of our kids
- Good control must be balanced with:
  - Risk of hypoglycemia
  - Participation in all age appropriate activities

Epidemiology of Type 1

- INCIDENCE: 15/100,000 American children per year
  - 1M children in PCMC catchments area, 150 new cases per year (we actually have more)
- PREVALENCE: 1/400 by the age of 15 yrs.
  - Estimate 2500 in PCMC casement
- Peak occurrence at ages 5-7 and at puberty
- Incidence is increasing with the most marked increase in ages < 5 years

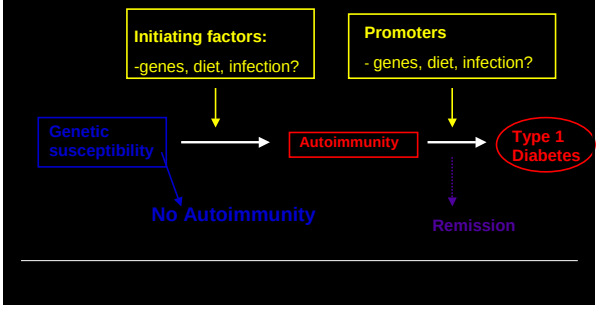
Genetic Susceptibility

- Increased risk to first degree relatives
  - Risk increases 10 fold, to 5-10%
  - Risk greater if father has diabetes
- HLA type
  - HLA-D3/4 increased risk in Caucasians
  - DQA1*0301, DQB1*0302, DQA1*0501, DQB1*0201 loci confer increased risk in Caucasians
  - Different types may be associated with different age at presentation and course

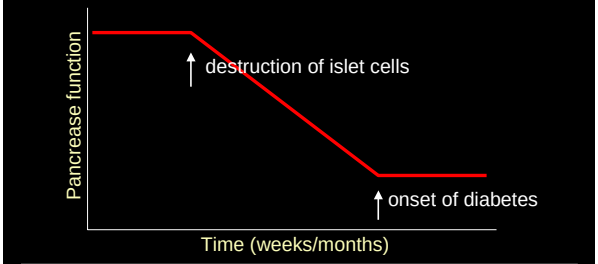
Autoimmunity

- DAISY
  - One or more antibodies present in 85-90% at time of diagnosis
  - Autoimmunity may develop at very young age and precede development of diabetes by years
  - Antibody titers may vary over time
- Antibodies associated with type 1 DM
  - GAD (glutamic acid decarboxylase)
  - IAA (insulin autoantibody)
  - ICA512 (tyrosine phosphatase)

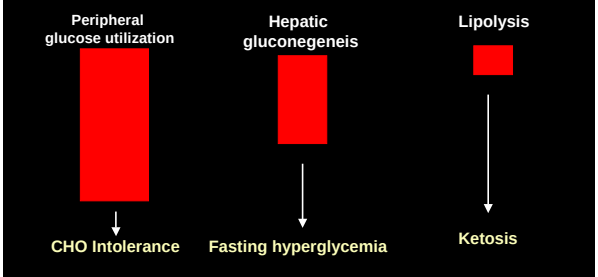
Steps Leading to Type 1



Onset of Diabetes



Metabolic Effects of Insulin



DKA

- State of absolute or relative insulin deficiency resulting in hyperglycemia and metabolic acidosis
  - Hyperglycemia - glucose >300 mg/dl
  - Acidosis - pH < 7.3
- Incidence is decreasing in new diagnosis
- Mortality is real, probably less than 1% in experienced hands, not always predictable

Etiology of DKA

- Hormonally mediated factors:
  - Insulin deficiency results in catabolic state
  - Counterregulatory hormone excess which accelerates catabolism
    - glucagon, cortisol, catacholamines, GH
  - Neither is sufficient
- Incidence: presenting event for 30-40% of new onset diabetes
  - Probably actually less with education
- Morbidity: 65% of all pediatric diabetic admissions

Treatment of DKA

- Standardized protocols
  - Careful fluid resuscitation – age appropriate volumes
  - Insulin infusion – IV drip at 0.1 units/kg/hr
  - Frequent blood glucose and electrolyte monitoring
- Attention to complications
  - Cerebral edema, hypocalcemia, hypokalemia

Summary

- Most children do very well and recover in 12 - 24 hours, but it is potentially fatal
- There is no substitute for close monitoring of child and labs; use ICU if there is any question or very young child
- Family needs to know severity of illness
  - Severe DKA should never happen again with appropriate home care

New Diagnosis

- Inpatient education program at PCMC
  - Accomplish education of family in 3 days
  - Pathophysiology and etiology
  - Insulin dosing, insulin injections, and meal planning
  - Treatment of emergencies
- Outpatient phone contact every 1-2 days over the first 2-4 weeks
- Office visit to continue education at 2-4 weeks
  - Sick days and blood ketone testing, correction dosing, trend and pattern analysis

Goals of Pediatric Care

- Enable children/teens to participate in all age appropriate activities with their peers
- Risk:Benefit Ratio of Control
  - Maintain good to excellent control of diabetes
  - Minimize the episodes of hypoglycemia

Type 1 Diabetes: Treatment

- Replacement of insulin
  - Must be administered by injection
  - Must be coordinated with food intake
- There is little usual routine anymore
  - Used to be 3 injections/day
  - Now at least 3 injections and may be as many as 7
  - Goal is to individualize therapy so as to minimize the intrusion into life

Changes in Approach

- Intensify control
  - DCCT results and impact upon long term complications
- Increase monitoring
  - Lunch time testing
  - More frequent testing
  - Testing at different times
- Increase insulin injections
- Increase flexibility

Intensive Regimens

- Multiple dosing regimens
- Generally means more testing and more shots
  - Can be done safely even in young children
  - Must use age appropriate targets and adjust for individuals, prevent hypoglycemia
- Increases flexibility

Types of Insulin

- Long acting:
  - Glargine
  - Ultralente
- Intermediate acting:
  - NPH
  - Lente
- Short acting:
  - Humalog™, Novalog™
  - Regular
- Premixed:
  - 70/30, 75/25

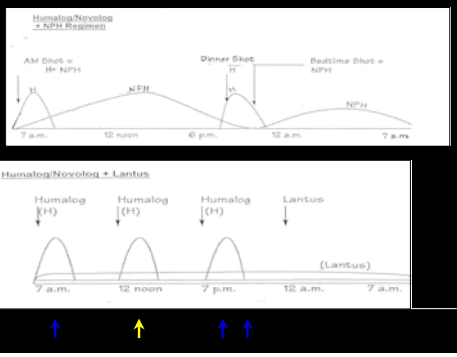
Designer Insulins

- Humalog® (Lilly, LysPro insulin) and Novalog ® (NovoNordisc,
  - Rapid onset, short duration
  - Match with food intake
- Lantus® (Aventis, Glargine)
  - Longer acting, no significant peak
  - Works for about 80-90% of people
  - Multiple different uses in peds

Insulin Administration

- Insulin must be coordinated with food
- Dose will vary with blood glucose level, food intake, and exercise
- Traditionally, use of NPH eliminated routine administration of lunchtime shot
  - More frequent use of pumps and lantus insulin means more children need a lunch shot of insulin
  - Lunch shots require calculation of insulin dose
    - Cover carbohydrate content and correct “out of range” blood glucose

Insulin Dosing



Insulin Dosing with NPH

- Mixed dosing of intermediate and short acting
  - TID dosing: mix of long and short acting
  - Mixed dose before breakfast, short acting before supper and long acting at hs
- Requires lunch be consistent with respect to time and amount of carbohydrate
  - Lunch injections prn hyperglycemia

Meal Schedule on NPH

- 3 meals and 2-3 snacks
  - Mid-morning snack in young children
  - Requires structure and consistent carbohydrate intake
- Blood sugar checks
  - Before meals
  - Before bedtime snack
  - PRN

NPH Example

- Assume a 30 kg 8 year old
- Meals
  - Breakfast and lunch 60 grams of carbs, dinner 45 grams, afternoon and bedtime snack of 30 grams
- Insulin
  - Breakfast: 15 units NPH and 5 units novalog
  - Dinner: 1 unit of novalog per 15 grams of carbs
  - Bedtime: 8 units NPH
  - Correction for high glucose: 1 unit of novalog per 50 mg/dl over 150

Insulin Dosing: Lantus®

- Lantus provides 20-24 hour background or basal coverage
- Additional insulin given at times of food intake
  - Meals and snacks
  - Dose for carbohydrate intake and correction of high glucose
- Increased injections provide increased flexibility
  - Both schedule and intake of food

Lantus Example

- Assume a 60 kg adolescent
- Meals: ad lib
  - But must be able to calculate carb content
- Insulin:
  - Lantus, 30 units sc q hs (9-10 PM)
  - Novalog = carb dose + correction at all meals and snacks
    - Carb dose: 1 unit of novalog per 10 grams of carbs
    - Correction dose: 1 unit of novalog per 25 mg/dl over 120 (no more often than q 3 hours)

Insulin Dosing: Pump

- More intensive management than NPH
  - More flexibility
  - Similar to Lantus insulin
- CSII or insulin pump
  - Continuous sc infusion of short acting insulin
  - Requires calculation of both a carbohydrate dose for food and correction dose
- In event of pump malfunction, have only 3-4 hours of insulin coverage

Blood Glucose

- Target range varies with age:
  - 100-200 mg/dl if age < 7
  - 80-180 mg/dl in 7-12 yo
  - 70-180 age > 12 years
- Target range is individualized
  - Modify based upon child's maturity and ability to recognize hypoglycemia (low blood sugar)
- Even in the best of all worlds, no one can achieve target range 100% of the time

Getting Control

- Blood sugar checks 4-6 times/day
  - Before meals, before bedtime and prn
- Written records
- Regular review of numbers
  - Contact with Diabetes office
  - Insulin dose changes usually no more than 1-2 times/week
- Control is not achieved instantaneously

Intensify Control

- Increase monitoring
  - Meters: smaller blood volume and faster results
  - Computer downloading at home
  - Non-invasive monitors
    - Trends not absolutes, still requires fingerpokes
- Flexibility
  - Increase the number of injections
  - New insulins

Post Prandial Blood Sugars

- Increased awareness of role of Post-prandial blood sugars in elevating $HgbA_1C$
- Target of the DCCT: <180 mg/dl
  - Age dependent targets
    - Age <5 yo: <200 mg/dl
    - Age 5-11 yo: <180 mg/dl
    - Age 12-18 yo: < 150 mg/dl
  - Test 1-2 hours after eating

Long Term Management

- Blood glucose checks at least 4 times a day every day
  - Occasional post meal and overnight checks
- Insulin injections 3-6 times per day, every day
  - Dose calculated for blood glucose and food intake
- Quarterly office appointment
  - Hgb A_1C, review of blood glucose records
- Regular educational updates from CDE re: blood glucose management, meal planning
- Complication screening as adolescents
  - Renal, Eye, Lipid, Neurologic

Hypoglycemia

- Exercise
- Driving
- Alternate site testing

Hypoglycemia: Blood sugar < 50

- Alert, able to cooperate and take po
  - 15-15 rule: 15 gms carbohydrate and recheck BS in 15 min.
  - give snack if not eating within 30 min.
  - Check on child later
  - Notify parent
- Unconcious
  - glucagon, glucose gel and call 911

Hypoglycemia: Blood sugar 50-70

- Important not to overtreat:
  - 15-15 rule, follow with snack if not eating within 30 min.
- No one can prevent all lows.
  - Recurrent episodes may be preventable
  - Recurrent episodes may be evident as poor school performance
- Never send child out of classroom alone

Hypoglycemia Treatment

- Low dose glucagon
  - May help prevent ER visits for mild hypoglycemia
  - Dilute glucagon and give 1 unit per year of age with insulin syringe
  - Can repeat in 20 minutes
- Severe hypoglycemic episode
  - Use standard dose of glucagon

Hyperglycemia: Blood sugar > 300

- Send home only if there are other problems, eg. vomiting
  - Check urine ketones
    - Moderate or large ketones requires more aggressive treatment, eg. additional insulin
- Hydrate with sugar free liquids
  - allow access to water and bathroom
  - prevent dehydration in hot weather
- Do not withhold food

Hyperglycemia

- Does not require leaving school
- Allow free access to water and bathroom
- Check ketones if blood sugar >300
  - If ketones large, child needs extra insulin, call parent(s) to come and get child
- Notify parent of blood sugar

Ketones

- Blood vs urine
  - Either can be used
  - Urine is easier
- Pitfalls of blood ketones
  - Does not equal urine testing
  - Technological difficulties, false readings
  - Only one meter, requires another type of strip and second finger poke

Limitations

- Avoid hypoglycemia
  - Deteriorating school performance
  - Hypoglycemia unawareness
  - Target ranges vary with age and circumstances
- Independence
  - Insulin pens
  - Responsibility: will the child do lunch glucose and dose insulin independently? Attend to pump alarms?
- Communication
  - Important to relay blood glucoses home; dosages are adjusted upon patterns not single values
  - Important to relay schedule changes to family for dose adjustment

Long Term Issues

- $HgbA_1C$ quarterly
  - Average of blood glucose (measured and not measured)
  - Target range varies with age
    - 7.5% - 8.5%
    - Must allow for growth
- Normal growth and development
- Associated disorders
  - Thyroid and Celiac

Psychological Issues

- Depression
- Needle phobias
- Eating disorders: male and female

Fitting In Diabetes

- Intensive therapy
  - Pump
  - Lantus
- Balance tight control with risk of hypoglycemia and lifestyle

Type 1 Prevention

- Making progress to better understanding of disease etiology and development
- Need to find low risk therapy
- Need to identify at risk individuals prior to- or very early in- course of disease

Why Haven't we Prevented Type 1?

- Smoldering course
  - Hard to identify those at risk early; therefore, hard to intervene early
  - Cost of screening
- Treatment of children
  - Need interventions with excellent safety profile
  - Need accurate methods of disease prevention so as not to treat unnecessarily
- Poor understanding of immune mechanisms
  - Need better understanding of immunology
  - Redundancy of immune cascades

Diet: Cow's Milk Protein

- Early introduction of cow's milk protein
  - Ongoing study in Europe (TRIGER)
  - DAISY: no correlation between cow's milk exposure and diabetes (JAMA, 2003)
  - BABYDIAB: no association with cow's milk (JAMA, 2003)
- Currently no evidence to implicate cow's milk exposure in development of type 1 DM

Diet: Cereals

- BABYDIAB:
  - Gluten exposure age <3 months: hazard ration of 4 (CI=1.4-11.5; n= 4 positive children)
  - No increase risk with exposure age >6mo.
  - No increase risk of celiac disease associated antibodies
  - All positives had high risk HLA allele
- DAISY:
  - Cereal exposure age <3 months: hazard ration of 4.3 (CI= 2-9.3)
  - Cereal exposure age > 7 months: hazard ratio 5.5 (CI= 2-13.8)
  - Adjusting for HLA, family history, etc. ratio of 5.5 and 12.5 respectively
  - 34 positive and 16 developed diabetes

Infection

- Viral
  - Enterovirus ?
  - Polio
  - Rubella
- Mycotoxins ?
- Immunizations
  - No current data to implicate immunizations

Clinical Education

- Pump preparation
  - Monthly, 12-15 families / class
- Intensive management
  - Twice a month, 4-6 families / class
- Individual education consultation
  - Weekly, 8 patients / week
- Pump Initiation
  - Weekly, 2-3 patients / week
- Medical Nutrition Consultation
  - Endocrine and Diabetes patients, weekly, 3 patients / week
- Diabetes Management in the School
  - With Pediatric Education Services at PCMC, twice a year
- Physician education programs

Future Programs

- Basic Carb Counting
- Recharge your D batteries
  - For older children/teens becoming more independent, twice in summer
- Advanced pump class
  - 6 times/year
- Patient / Parent support groups – quarterly
- Transitioning to independence
  - Adolescents ready to move to adult medicine program - twice a year

Future Technology

- Pumps and meters that communicate
  - Bolus wizard software
  - "Beam" BG to pump
- Implantable pump / BG sensor
- Non-invasive BG monitors
- Cure
  - Immune system very complex
  - Good, low risk treatment means "cure" must be have excellent risk: benefit profile

How Are We Doing?

- IHC care process model
  - Education programs for both initial and ongoing management
  - Outcome measures to be monitored through health systems database
- State Department of Health care guidelines
  - Outcome measures

Summary

- With the exception of severe low blood sugar, children should not be sent home because of their diabetes
- Good control requires school, family, and MD participation
- If you have questions re: student's care, we will be happy to discuss problems / concerns (with parental permission)

Summary

- Control of the diabetes is individual
  - As much as you or I might want intensive management, not all children/families are able to do it
- Compromise is needed to achieve the best control possible for any one child

Questions??????